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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/755,639	01/12/2004	John P. Wikswo	14506-44211	1080
24728 7590 05/15/2007 MORRIS MANNING MARTIN LLP 3343 PEACHTREE ROAD, NE 1600 ATLANTA FINANCIAL CENTER ATLANTA, GA 30326			EXAMINER BOWERS, NATHAN ANDREW	
			ART UNIT 1744	PAPER NUMBER
			MAIL DATE 05/15/2007	DELIVERY MODE PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No. 10/755,639	Applicant(s) WIKSWO ET AL.	
	Examiner Nathan A. Bowers	Art Unit 1744	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
 - If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
 - Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 03 August 2006.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-74 is/are pending in the application.
- 4a) Of the above claim(s) 25-74 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1-24 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☒ The drawing(s) filed on 12 January 2004 is/are: a) ☒ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413) |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | Paper No(s)/Mail Date. _____ |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08) | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| Paper No(s)/Mail Date <u>011204</u> . | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

Election/Restrictions

Applicant's election with traverse of Group I, claims 1-11 in the reply filed on 03 August 2006 is acknowledged. The traversal is on the grounds that there is no serious burden on the Examiner. Upon reexamination of the restriction requirement, Group II, claims 12-24 will be examined along with Group I, claims 1-11. A revised and corrected restriction requirement is outlined below.

Restriction is required under 35 U.S.C. 121 and 372.

This application contains the following inventions or groups of inventions which are not so linked as to form a single general inventive concept under PCT Rule 13.1.

In accordance with 37 CFR 1.499, applicant is required, in reply to this action, to elect a single invention to which the claims must be restricted.

Group I, claim(s) 1-24, drawn to a device for monitoring the status of at least one cell.

Group II, claim(s) 25-30, drawn to a method for monitoring the status of at least one cell.

Group III, claim(s) 31-36 and 43-48, drawn to a device for monitoring the status of at least one cell.

Group IV, claim(s) 37-42 and 49-60, drawn to a method for monitoring the status of at least one cell.

Group V, claim(s) 61-72 and 74, drawn to a device for controlling the physiological status of at least one cell.

Group VI, claim(s) 73, drawn to a method for controlling the physiological status of at least one cell.

The inventions listed as Groups I-VI do not relate to a single general inventive concept under PCT Rule 13.1 because, under PCT Rule 13.2, they lack the same or corresponding special technical features. The Anderson (US 20010036672) and Dodgson (US 20030107386) each disclose a device comprising a first, second and third substrates forming first and second passages. As evidenced by these references, the structural configuration set forth in claim 1 is known in the art, and therefore does not constitute a special technical feature.

The requirement is still deemed proper and is therefore made FINAL.

Claims 25-74 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected species, there being no allowable generic or linking claim. Applicant timely traversed the restriction (election) requirement in the reply filed on 03 August 2006.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

- 1) Claims 1, 2, 5, 8 and 10 are rejected under 35 U.S.C. 102(b) as being anticipated by Anderson (US 20010036672).

With respect to claim 1, Anderson discloses a device comprising a first substrate (Figure 2:116) having a first and second surface, and a second substrate having a first and second surface. The second substrate is composed of a first planar member (Figure 2:106) and a corresponding membrane (Figure 2:112) that are mated together to form the bottom wall of a reaction chamber (Figure 2:104). The body portion of the second substrate defines a first passage (Figure 2:110) that flows between the first and second side surfaces of the second substrate. An opening (Figure 2:108) is provided on the second substrate that is in fluid communication with the first passage and the reaction chamber. Sidewalls (Figure 2:102) and a third substrate are provided above the second substrate to further define the reaction chamber, and to form a second passage (Figure 2:118). This is described in paragraphs [0105]-[0109]. Paragraphs [0066], [0067], [0147] and [0169] state that a variety of pH and temperature sensors are provided in the reaction chamber. The apparatus of Anderson is considered fully capable of being used to monitor the status of at least one cell positioned within the reaction chamber.

With respect to claim 2, Anderson discloses the apparatus in claim 1 wherein the cell defines an opening through which the intracellular space of the cell is in fluid communication with the first passage. All biological cells comprise a plurality of

naturally formed pores that allow the passage of compounds through the cell membrane.

With respect to claim 5, Anderson discloses the apparatus in claim 2 wherein the apparatus is fully capable of introducing a first and second medium into the chamber through the first and second passages. PH sensors disclosed by Anderson are fully capable of determining a cell reaction in response to compounds contained within the first and second medium.

With respect to claim 8, Anderson discloses the apparatus in claim 1 wherein valves are provided for regulating the flow of fluids through the first chamber. This is described in paragraph [0018] and throughout the reference.

With respect to claim 10, Anderson discloses the apparatus in claim 1 wherein the first passage is in communication with a medium reservoir. Anderson teaches the use of supply fluid reservoirs in paragraph [0120].

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

The factual inquiries set forth in *Graham v. John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

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1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

- 2) Claims 1-4, 6 and 8-11 are rejected under 35 U.S.C. 103(a) as being unpatentable over Dodgson (US 20030107386).

With respect to claims 1 and 2, Dodgson discloses a device for monitoring the status of at least one cell. The apparatus comprises a first substrate, a second substrate supported by the first substrate, and a first passage formed within the body of the second substrate. An opening is formed on the first surface of the second substrate such that the first passage is in fluid communication with a reaction area formed above the second substrate. Paragraphs [0009] and [0010] state that electrodes (Figure 3:24,26) are provided to detect the presence of a cell (Figure 3:16) to be tested. A third substrate is positioned above the second substrate to define a reaction area

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therebetween, and a second passage is formed below the third substrate in fluid communication with the reaction area. This is apparent from Figure 3. Another embodiment in Figure 4 depicts a similar apparatus, however, the third substrate is replaced with a sidewall feature. Dodgson does not expressly describe an embodiment in which a third substrate and sidewalls are both formed above the second substrate to define a reaction chamber and a second passage.

Fig.3.

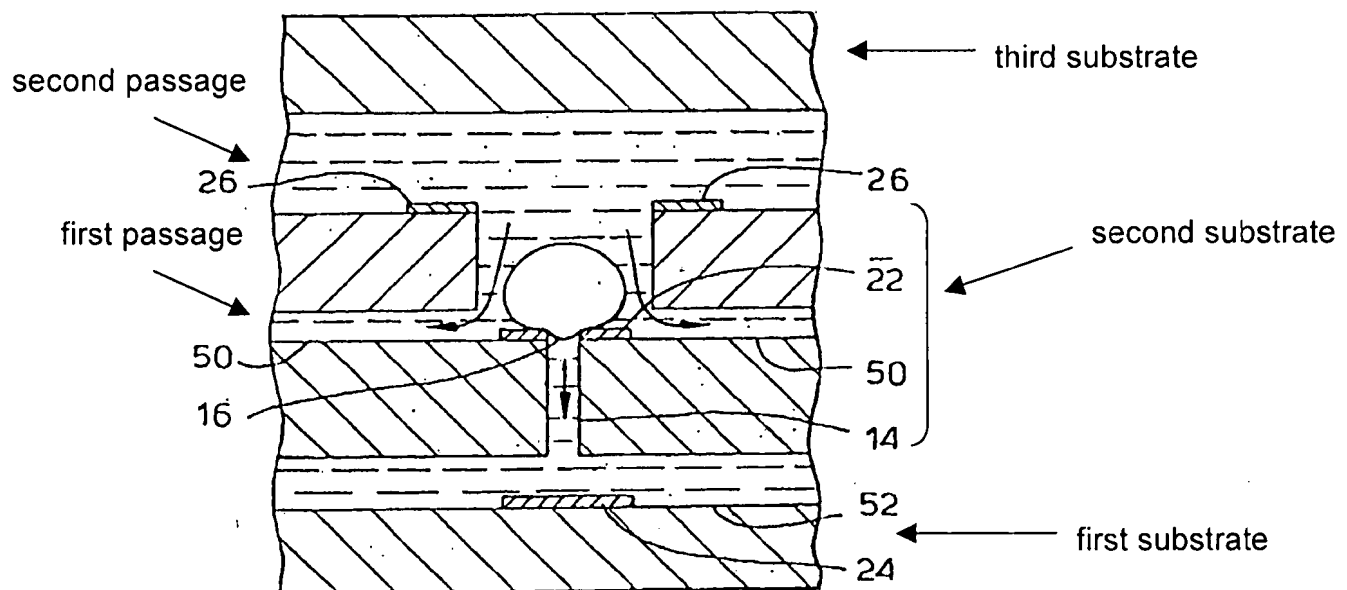
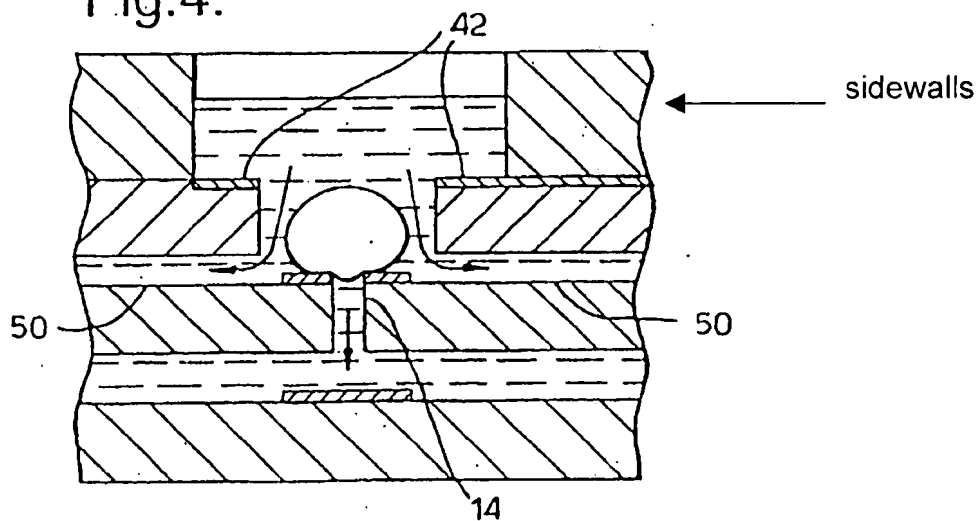


Fig.4.



At the time of the invention, it would have been obvious to alter the construction of Dodgson's device by incorporating features set forth in the embodiments presented in Figures 3 and 4. It would have been apparent to provide a reaction chamber defined by

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both a third substrate and sidewalls, as such construction is considered to be well known and commonly practiced in the art. It would require only minor structural alterations to either of the presented embodiments to form a reaction chamber and second passage bound by both a sidewall area and a third substrate.

With respect to claims 3, 4 and 6, Dodgson discloses the apparatus set forth in claim 2 as set forth in the 35 U.S.C. 103 rejection above. In addition, Dodgson states that the electrode sensing elements further act as an electroporation device capable of stimulating cells positioned within the reaction area. This is taught in paragraph [0039]. A medium is introduced to the reaction area through the second passage such that the sensor measures the response of the cell to the medium. Paragraph [004] states that variations in the medium cause a variation in the impedance of the cell in the reaction area.

With respect to claims 8 and 9, Dodgson discloses the apparatus set forth in claim 1 as set forth in the 35 U.S.C. 103 rejection above. Dodgson additionally indicates that control devices are provided at the first and second passages to regulate fluid flow. Paragraph [0043] describes the use of valves. Valves are considered to be well known in the art.

With respect to claims 10 and 11, Dodgson discloses the apparatus set forth in claim 1 as set forth in the 35 U.S.C. 103 rejection above. Although Dodgson does not

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expressly disclose the use of reservoirs in communication with the first and second passages, it is understood that the use of reservoirs as supply medium containers and waste containers is notoriously well known in the art. It would have been obvious to equip the apparatus of Dodgson with reservoirs in order to perfuse a solution through the system in a continuous nature.

With respect to claims 12-15, 17, 19 and 21-24, Dodgson discloses the apparatus as previously described above. Dodgson additionally states in paragraphs [0010], [0013] and [0014] that a plurality of chambers are defined by the first, second and third substrates. An array of chambers is formed such that each chamber includes a sensor/poration electrode capable of detecting impedance and electrically stimulating a cell. Each chamber is connected to neighboring chambers via the second passage formed by the third substrate and the sidewalls.

3) Claims 6, 7, 9 11-13 and 16-24 are rejected under 35 U.S.C. 103(a) as being unpatentable over Anderson (US 20010036672).

With respect to claims 6, 7, 9 and 11, Anderson discloses the apparatus set forth in claims 1 and 2 as set forth in the 35 U.S.C. 102 rejections above. As previously noted, Anderson teaches the use of valves and sample reservoirs to regulate fluid flow through the apparatus. Anderson, however, does not expressly indicate that the second passage is used to deliver fluids to the reaction chamber. Rather, Anderson suggests that the second passage should be used as a gas vent.

At the time of the invention, it would have been obvious to either utilize the second passage disclosed by Anderson as a fluid port, or to add an extra fluid passage through the sidewalls and third chamber in addition to the second passage. The construction of fluid passages through substrates and sidewalls is considered to be well known in the microfluidic chip art. It would have been beneficial to add fluids to the reaction chamber via a second passage because this would have allowed one to simultaneously test the effects of multiple compounds on analytes within the chamber.

With respect to claims 12, 13 and 16-24, Anderson discloses the apparatus as previously described above. Anderson teaches that a plurality of chambers are linked in series via the first passage (Figure 2:110) formed within the second substrate. This is described in paragraphs [0039], [0109] and [0110]. Anderson, however, does not expressly disclose that a second passage formed by the third substrate and the sidewalls is also used to connect the plurality of chambers in such a way that each chamber is in fluid communication with neighboring chambers.

At the time of the invention, it would have been obvious to create a second passageway defined by the third substrate and the sidewalls of each of the plurality of chambers in the apparatus of Anderson. It would have been apparent to use this second passageway to deliver fluids to each of the chambers in a manner similar to that of the first passageway. Clearly, Anderson understands the benefits of being able to move analytes and test compounds between a plurality of serially linked chambers, as evidenced by the construction of the first passageway. The incorporation of a second

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passageway capable of complimenting the function of the first passageway would merely require the duplication of parts already described by Anderson.

Conclusion

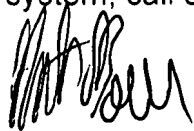
The prior art made of record and not relied upon is considered pertinent to applicant's disclosure. The Juncosa (US 6225109) reference discloses the state of the art regarding the formation of a plurality of chambers using first, second and third substrates.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Nathan A. Bowers whose telephone number is (571) 272-8613. The examiner can normally be reached on Monday-Friday 8 AM to 5 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gladys Corcoran can be reached on (571) 272-1214. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

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Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.



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